REMARKS

Amendments to the specification

The specification has been amended for clarity and to correct typographical errors. No new matter is introduced by the amendments to the specification, which are fully supported by the application as originally filed.

For amended paragraphs 12 and 32, "MHC" has been corrected to read "MCH." Support for the recitation of "MCH" is found, *inter alia*, on page 5, lines 1-2 of the originally filed specification.

For amended paragraphs 12, 16, 19, 32, and 38, "mean cell hemoglobin" has been corrected to read "mean cell hemoglobin content" which is generally accepted in the hematological arts to correspond to the acronym MCH. See attached reference: Katyukhin et al., 1998, "Rheologic properties of mammalian erythrocytes: relationship to transport ATPases" *Comp. Biochem. Physiol. B. Biochem. Mol. Biol.* 120(3):493-8.

For amended paragraphs 12, 13, 26, and 27, support for the recitation of "whole blood concentration" is found, *inter alia*, on page 20, lines 10-16, and on page 20, lines 30-32 to page 21, lines 1-9 of the originally filed specification.

For amended paragraphs 12 and 13, support for the recitation of "red blood cell derived hemoglobin" and "cell derived hemoglobin" is found, *inter alia*, on page 3, lines 12-18; on page 9, lines 1-7; and on page 9, lines 26-31 to page 10, lines 1-2 of the originally filed specification.

For amended paragraph 18, support for the recitation of "correct for interference" and "allow accurate determination" is found, *inter alia*, on page 5, lines 28-31 to page 6, lines 1-2 of the originally filed specification.

For amended paragraph 24, support for the recitation of "plasma hemoglobin concentration" is found, *inter alia*, on page 9, lines 26-31 to page 10, lines 1-2; and on page 20, lines 26-32 of the originally filed specification.

For amended paragraph 38, support for the recitation of "for MCH," "calculated HGB," and "for MCHC" is found, *inter alia*, on page 17, lines 7-20 of the originally filed specification. Support for the recitation of "(MCHC)" is found, *inter alia*, on page 4, lines 20-26 of the originally filed specification.

Amendments to the claims

Claims 1-3 and 5-24 are pending in the application.

Claim 4 has been cancelled without prejudice or disclaimer solely to expedite the patent application process in accordance with the PTO's Patent Business Goals, 65 Fed. Reg. 54603 (September 8, 2000). Applicants reserve the right to present the cancelled subject matter in a co-pending application.

Claims 1-2, 5-11, 12, 14-19, and 21 have been amended to correct typographical errors, to clarify and/or to more fully encompass Applicant's invention. The subject matter of the amended claims is fully supported by the specification and claims as originally filed.

For amended claim 1, support for the recitation of "blood sample" is found, *inter alia*, on page 11, lines 12-14 of the originally filed specification. Support for the recitation of "other sample having red blood cells" is found, *inter alia*, on page 9, lines 26-31 to page 10, lines 1-2 of the originally filed specification. Support for the recitation of "determined by cell-by-cell measurements" is found, *inter alia*, on page 19, line 32 to page 20, lines 1-2 of the originally filed specification. Support for the recitation of "picograms/cell" is found, *inter alia*, on page 5,

lines 12-18 of the originally filed specification. Support for the recitation of "(gm/dL)" is found, *inter alia*, in original claim 9, and on page 13, lines 18-30 of the originally filed specification. Support for the recitation of "comprises" is found in original claim 12.

For amended claims 1 and 9, support for the recitation of "for interference in" is found, *inter alia*, on page 18, lines 19-22.

For amended claims 1, 9, and 21, "mean cell hemoglobin" has been corrected to read "mean cell hemoglobin content" which is generally accepted in the hematological arts to correspond to the acronym MCH. See Katyukhin et al.

For amended claims 1, 2, 9, 10, 12, 15, 16, 17, and 19, support for the recitation of "exogenous heme-colored blood substitute" is found, *inter alia*, on page 7, lines 23-28, and on page 8, lines 6-19 of the originally filed specification.

Claim 2 has been amended to conform to amended claim 1.

Claim 5 has been amended to correctly depend from claim 3.

Claims 7, 10, and 17 have been amended to cancel non-elected subject matter in compliance with the election requirement for the application. Applicants reserve the right to present the cancelled subject matter in a co-pending application.

Claims 8, 11, and 18 have been amended to conform to amended claims 7, 10, and 17.

For amended claim 9, support for the recitation of "is analyzed on" is found, *inter alia*, in original claim 1. Support for the recitation of "comprises" is found in original claim 12. Support for the recitation in "thereby correcting" is found, *inter alia*, on page 6, lines 20-27 of the originally filed specification.

Claim 19 has been amended to conform to the subject matter encompassed by claims 15 and 16.

For amended claim 21, "MHC" has been corrected to read "MCH." Support for the recitation of "MCH" is found, *inter alia*, on page 5, lines 1-2 of the originally filed specification.

Claim 24 has been newly added to more fully encompass Applicant's invention. For added claim 24, support can be found, *inter alia*, on page 13, lines 18-30 of the original specification.

It is noted that the amendments to the claims and specification have been depicted in accordance with the revised format authorized by the Pre-OG Notice at http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/revamdtprac.htm. Additions are shown by double underlining; deletions are shown by strikethrough.

Claim objections

Claim 9 has been objected to for an informality (Office Action, page 2). The Examiner states that Claim 9 is missing a closed parenthesis on line 30, which requires appropriate correction (Office Action, page 2). As amended herein, claim 9 includes the closed parenthesis that was previously omitted. Withdrawal of this objection is therefore respectfully requested.

35 U.S.C. § 112, second paragraph

Claims 1-23 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention (Office Action, page 2). The Examiner states:

- Claim 1 is vague and indefinite due to the phrase "blood, plasma, or sample containing heme-colored interfering substance";
- Claims 7, 10, and 17 contain non-elected subject matter;

- Claim 9 is confusing, since the recited system is meant to "alert" a practitioner to a "need" to correct MCH and MCHC, but there are no alerting limitations in the claim, and it is unclear why altering is required in a system where there is automatic correction;
- Claim 14 is as vague and indefinite because it is unclear what unit corrections correspond to 10 or 100;
- Claim 16 is vague and indefinite due to the phrase "recovers the original blood chemistry result"; claims 9 and 15 contain the same unclarity issue; and
- Claims 10-14, and 17-23 are dependent on the rejected claims, and therefore are also rejected (Office Action, pages 2-4).

Applicant respectfully traverses this rejection. As indicated above, claim 4 has been cancelled, and claims 1, 7, 9, 10, 14-16, and 17 have been amended as a result of this Amendment. In particular:

- Claim 1 has been amended to recite the phrase "blood sample which comprises an exogenous blood substitute";
- Claims 7, 10, and 17 have been amended to delete the non-elected subject matter;
- Claim 9 has been amended to include alerting limitations in the claim, and clarify that the practitioner is being alerted to the corrected MCH and MCHC values;
- Claim 14 has been amended to delete the phrase "to correct for units of dimensions"; and
- Claim 16 has been amended to delete the phrase "recovers the original blood chemistry result"; claims 9 and 15 have been similarly amended.

As presently amended, claims 1, 7, 9, 10, 14-16, and 17 read:

1. An automated method for correcting for interference in mean cell hemoglobin content (MCH) and mean cell hemoglobin concentration (MCHC) values in a blood sample or other sample having red blood cells, wherein the sample comprises an exogenous heme-colored blood substitute and is analyzed on an automated hematology analyzer, comprising:

(a) dividing cellular hemoglobin concentration (gm/dL), determined by cell-by-cell measurements, by red blood cell concentration (cells/mm3);

(b) multiplying the value of (a) by a first constant to correct for differences in units of dimensions to obtain a corrected mean cell hemoglobin content (MCH) value (picograms/cell);

(c) dividing the cellular hemoglobin concentration (gm/dL), determined by cell-by-cell measurements, by the hematocrit (HCT), (%), value; and

(d) multiplying the value of (c) by a second constant to correct for differences in units of dimensions to obtain a corrected mean cell hemoglobin concentration (MCHC) value (gm/dL); thereby correcting for interference in the mean cell hemoglobin content (MCH) and mean cell hemoglobin concentration (MCHC) values in the sample.

7. The method according to claim 2, wherein the extracellular hemoglobin product or the oxygen-carrying blood substitute is recombinant human hemoglobin.

9. A system for correcting mean cell hemoglobin content (MCH) and mean cell hemoglobin concentration (MCHC) values in a blood sample which comprises an exogenous heme-colored blood substitute and is analyzed on an automated hematology analyzer, comprising:

a) labeling a blood collection container to indicate that the blood sample contained therein comprises an exogenous heme-colored blood substitute;

b) correcting automatically for interference in mean cell hemoglobin content (MCH) and mean cell hemoglobin concentration (MCHC) values based on the labeling indication of (a), wherein said correction is performed by the automated analyzer and comprises formula (1):

(1) MCH (corrected), (picograms/cell) =
Cellular hemoglobin (gm/dL) (x constant to correct for units of dimensions)
Red Blood Cell concentration (cells/mm3);

and formula (2):

(2) MCHC (corrected), (gm/dL) =
Cellular hemoglobin (gm/dL) (x constant to correct for units of dimensions)
HCT (%);

and thereby correcting mean cell hemoglobin content (MCH) and mean cell hemoglobin concentration (MCHC) values in the sample.

10. The system according to claim 9, wherein the exogenous heme-colored blood substitute is an oxygen-carrying hemoglobin substitute.

14. The system according to claim 9, wherein the constant in formula 1 is 10, and the constant in formula 2 is 100.

15. A method for automatic correction of interference in a blood chemistry value in a blood, plasma, or serum sample analyzed on an automated hematology analyzer, wherein said interference is due to the presence of an exogenous heme-colored blood substitute in the blood, plasma, or serum sample, comprising:

a) labeling a sample collection container to indicate that the sample contained therein contains the exogenous heme-colored blood substitute, wherein said label signals correction of the blood chemistry value; and

b) correcting automatically the blood chemistry value based on the labeling signal of (a), wherein the correction is performed by the automated hematology analyzer employing the plasma hemoglobin value automatically generated by the automated hematology analyzer; thereby correcting for interference in the analyzed sample.

16. A method for automatic correction of interference in a blood chemistry value in a blood, plasma, or serum sample, wherein said interference is due to the presence of an exogenous heme-colored blood substitute in the sample, comprising:

a) labeling a sample collection container to indicate that the blood, plasma, or serum sample contained therein contains the exogenous heme-colored blood substitute, wherein said label signals correction of the blood chemistry value; and

b) correcting automatically the blood chemistry value based on the labeling signal of (a), wherein the correction is performed by the automated analyzer employing the plasma hemoglobin value automatically generated by the analyzer; wherein the corrected chemistry value is determined by subtracting from the reported chemistry result the following product: (correction factor x plasma or serum hemoglobin value scaled to the appropriate units of dimensions of the reported analytes), thereby correcting for interference in the analyzed sample.

17. The method according to claim 15 or claim 16, wherein the exogenous heme-colored blood substitute is an oxygen-carrying hemoglobin substitute, recombinant human hemoglobin.

It is believed that these amendments obviate the rejection under 35 U.S.C. § 112, second paragraph, for claims 1, 7, 9, 10, 14-16, and 17, and claims dependent thereon, including claims 2-3, 5-6, 8, 11-13, and 18-23, as presented herein. Applicant respectfully requests withdrawal of this ground of rejection, and reconsideration of the rejected claims.

35 U.S.C. § 102(b)

Claim 1 has been rejected under 35 U.S.C. § 102(b) as being anticipated by Chupp et al., U.S. Patent No. 5,631,165 (Office Action, page 4). The Examiner states that Chupp et al. teach an automatic method for correcting MCH and MCHC in blood by performing the mathematical computations described in claim 1 (a)-(d) of the instant application (Office Action, page 4). The Examiner concludes that Chupp et al. teach all of the limitations of claim 1, and thereby anticipate the subject matter of the claim (Office Action, page 4). Applicant respectfully traverses this rejection.

Chupp et al. report methods and devices for performing automated blood cell analysis of whole blood samples (column 1, lines 15-21). However, in the Office Action, it is noted that Chupp et al. fail to teach the analysis of blood comprising an extracellular hemoglobin product or oxygen-carrying blood substitute such as recombinant human hemoglobin (Office Action, page 6). As presently amended, claim 1 is directed to an automated method of obtaining corrected MCH and MCHC values in blood sample comprising an exogenous heme-colored blood substitute. The amended claim reads, in part:

> 1. An automated method for correcting for interference in mean cell hemoglobin content (MCH) and mean cell hemoglobin concentration (MCHC) values in a blood sample or other sample having red blood cells, wherein the sample comprises an exogenous heme-colored blood substitute...

An exogenous heme-colored blood substitute is comparable to an extracellular hemoglobin product or an oxygen-carrying blood substitute. Because the Chupp et al. publication fails to teach the analysis blood comprising an exogenous heme-colored blood substitute, the publication fails to teach every element of claim 1 as presented herein. MPEP § 2131 indicates that a claim is anticipated only if each and every element as set forth in the claim

is found, either expressly or inherently described, in a single prior art reference. *See Verdegall Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Accordingly, it is submitted that the Chupp et al. publication does not anticipate the subject matter of claim 1 as presented herein. Applicant respectfully requests withdrawal of this ground of rejection, and reconsideration of the rejected claim.

35 U.S.C. § 103(a)

Claims 1-15 and 17-22 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Chupp et al., U.S. Patent No. 5,631,165, in view of Chang et al., U.S. Patent No. 5,200,323 (Office Action, page 5). The Examiner states that a skilled artisan would have been motivated to enhance the automated hematology analyzer and method of correcting MCH and MCHC values in blood, as stated by Chupp et al., including blood samples containing modified hemoglobin blood substitutes, as stated by Chang et al. (Office Action, pages 6-7). Applicant respectfully traverses this rejection.

Chupp et al. report methods and devices for performing automated blood cell analysis of whole blood samples (column 1, lines 15-21). Chang et al. report *in vitro* methods for determining the complement activation of modified hemoglobin blood substitutes upon addition to human plasma (column 4, lines 36-39). As indicated in the Office Action, Chupp et al. fail to teach the analysis of blood comprising an extracellular hemoglobin product or oxygen-carrying blood substitute such as recombinant human hemoglobin (Office Action, page 6). In addition, both Chupp et al. and Chang et al. fail to teach or suggest the correction of interference in blood, plasma, or serum samples comprising an exogenous heme-colored blood substitute.

Yet, claim 1 as presented herein is directed to:

1. An automated method for correcting for interference in mean cell hemoglobin content (MCH) and mean cell hemoglobin concentration (MCHC) values...

Claim 9 as presented herein is directed to:

9. A system for alerting a practitioner to corrected mean cell hemoglobin content (MCH) and mean cell hemoglobin concentration (MCHC) values in a blood sample which comprises an exogenous heme-colored blood substitute and is analyzed on an automated hematology analyzer, comprising:

a) labeling a blood collection container to indicate that the blood sample contained therein comprises an exogenous heme-colored blood substitute;

b) correcting automatically for interference in mean cell hemoglobin content (MCH) and mean cell hemoglobin concentration (MCHC) values...

Claim 15 as presented herein is directed to:

15. A method for automatic correction of interference in a blood chemistry value...

Because the Chupp et al. and Chang et al. publications fail to teach the correction of interference in blood, plasma, or serum samples comprising an exogenous heme-colored blood substitute, the publications fail to teach or suggest every element of claims 1, 9, or 15 as presented herein. MPEP § 2143.03 indicates that all of the claim limitations must be taught or suggested by the prior art to establish a *prima facie* case of obviousness. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Accordingly, it is submitted that a *prima facie* case of obviousness is not established for claims 1, 9, or 15, or dependent claims 1-3, 5-9, 10-14, and 17-22, as presented herein. As indicated above, claim 4 has been cancelled without prejudice or disclaimer. Applicant therefore respectfully requests withdrawal of this ground of rejection for claims 1-3, 5-15 and 17-22 in the application. Reconsideration of the rejected claims is respectfully requested.

CONCLUSION

Applicant believes that the claims of the subject application are in condition for allowance. An action passing this case to issue is courteously urged. In the event that the Examiner is of the opinion that further discussion of the application would be helpful, the Examiner is hereby respectfully requested to telephone the Applicant's undersigned representative at (212) 415-8721 and is assured of full cooperation in an effort to advance the prosecution of the instant application and claims to allowance.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for the timely consideration of this amendment under 37 C.F.R. §§ 1.16 and 1.17, or credit any overpayment to Deposit Account No. 13-4500, Order No. 0708-4057.

Respectfully submitted,
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